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 NEWS  3  JAN 25  Annual Reload of MEDLINE database
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                  Now Available for Download
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                  of Author Abstracts
 NEWS  6  FEB 16  New FASTA Display Formats Added to USGENE and PCTGEN
 NEWS  7  FEB 16  INPADOCDB and INPAFAMDB Enriched with New Content
                  and Features
 NEWS  8  FEB 16  INSPEC Adding Its Own IPC codes and Author's E-mail
                  Addresses
 NEWS  9  APR 02  CAS Registry Number Crossover Limits Increased to
                  500,000 in Key STN Databases
 NEWS 10  APR 02  PATDPAFULL: Application and priority number formats
                  enhanced
 NEWS 11  APR 02  DWPI: New display format ALLSTR available
 NEWS 12  APR 02  New Thesaurus Added to Derwent Databases for Smooth
                  Sailing through U.S. Patent Codes
 NEWS 13  APR 02  EMBASE Adds Unique Records from MEDLINE, Expanding
                  Coverage back to 1948
 NEWS 14  APR 07  CA/CAplus CLASS Display Streamlined with Removal of
                  Pre-IPC 8 Data Fields
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=> file caplus, biosis, embase, medline
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                                   ENTRY    SESSION
FULL ESTIMATED COST                           0.22       0.22

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FILE 'MEDLINE' ENTERED AT 14:51:16 ON 11 MAY 2010

=> s ("hMN-14" (n) "KLHuVhAIGA")
L1          0 ("HMN-14" (N) "KLHUVHAIGA")

=> s "hMN-14"
L2         90 "HMN-14"

=> duplicate remove L2
DUPLICATE PREFERENCE IS 'CAPLUS, BIOSIS, EMBASE, MEDLINE'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L2
L3          42 DUPLICATE REMOVE L2 (48 DUPLICATES REMOVED)
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=> s L3 and "KLHUVHAIGA"
L4          0 L3 AND "KLHUVHAIGA"

=> s L2 and "KLHu VhAIGA"
L5          0 L2 AND "KLHU VHAIGA"

=> s "KLHU VH AIGA
MISMATCHED QUOTE '"KLHU'
Quotation marks (or apostrophes) must be used in pairs,
one before and one after the expression you are setting
off or masking.

=> s L3 and (thyroid and colorectal)
L6          4 L3 AND (THYROID AND COLORECTAL)

=> duplicate remove L6
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KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L6
L7           4 DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)

=> d L7 bib abs 1-4

L7   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2010 ACS on STN
AN   2009:523786  CAPLUS
DN   150:441526
TI   PEGylation by dock and lock (DNL) technique
IN   McBride, William; Chang, Chien-Hsing; Rossi, Edmund; Goldenberg, David
PA   IBC Pharmaceuticals, Inc., USA
SO   PCT Int. Appl., 65 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 25
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   WO 2009055653        A1    20090430    WO 2008-US81085        20081024
         W:  AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,
             CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES,
             FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE,
             KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,
             ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH,
             PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ,
             TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
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IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 20090060862	A1	20090305	US 2007-925408	20071026
US 7666400	B2	20100223		
AU 2008316741	A1	20090430	AU 2008-316741	20081024
CA 2696160	A1	20090430	CA 2008-2696160	20081024

PRAI US 2007-925408	A	20071026
US 2005-668603P	P	20050406
US 2005-728292P	P	20051019
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US 2005-478021	A2	20060629
US 2006-478021	A2	20060629
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US 2006-864530P	P	20061106
US 2006-633729	A2	20061205
WO 2008-US81085	W	20081024

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention concerns methods and compns. for forming PEGylated complexes of defined stoichiometry and structure. In preferred embodiments, the PEGylated complex is formed using dock-and-lock technol., by attaching a target agent to a DDD (dimerization and docking domaine) sequence and attaching a PEG moiety to an AD (anchor domain) sequence and allowing the DDD sequence to bind to the AD sequence in a 2:1 stoichiometry, to form PEGylated complexes with two target agents and one PEG moiety. In alternative embodiments, the target agent may be attached to the AD sequence and the PEG to the DDD sequence to form PEGylated complexes with two PEG moieties and one target agent. In more preferred embodiments, the target agent may comprise any peptide or protein of physiol. or therapeutic activity. The PEGylated complexes exhibit a significantly slower rate of clearance when injected into a subject and are of use for treatment of a wide variety of diseases. The inventors have developed a platform technol. to utilize the DDD (dimerization and docking domain) of human RII.alpha. and the AD (anchor domain) of a certain amino acid sequence as an excellent pair of linker modules for docking any two entities, into a noncovalent complex, which could be further locked into a stably tethered structure through the introduction of cysteine residues into both the DDD and AD at strategic positions to

facilitate the formation of disulfide bonds. DNL-PEGylation of
IFN.alpha.2b results in improved and long-lasting efficacy, allowing for
less frequent dosing.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2000:226243 CAPLUS
DN 133:131853
TI Factors influencing tumor dosimetry in the radioimmunotherapy of CEA-expressing cancers with 131I-labeled murine and humanized anti-CEA monoclonal antibodies
AU Behr, T. M.; Sharkey, R. M.; Dunn, R. M.; Juweid, M. E.; Siegel, J. A.; Goldenberg, D. M.
CS Garden State Cancer Center at the Center for Molecular Medicine and Immunology, Newark, NJ, 07103, USA
SO International Radiopharmaceutical Dosimetry Symposium, Proceedings of a Conference, 6th, Gatlinburg, Tenn., May 7-10, 1996 (1999), Meeting Date 1996, Volume 1, 225-239. Editor(s): Schlafke-Stelson, Audrey T.; Stabin, Michael G.; Sparks, Richard B. Publisher: National Technical Information Service, Springfield, Va.
CODEN: 68TXAO
DT Conference
LA English
AB Achieving a sufficiently high radiation dose is probably the key to therapeutic success in radioimmunotherapy (RAIT) of solid tumors. The aim of this study was, therefore, to examine which factors influence tumor dosimetry in the RAIT of CEA-expressing cancers. Data from 119 tumors in 93 patients with CEA-expressing tumors (e.g., colorectal, lung, breast, ovarian, pancreatic, and medullary thyroid carcinomas) were analyzed. They underwent RAIT with the 131I-labeled IgG1 anti-CEA antibodies NP-4 (Ka=108M-1), MN-14 (Ka=109M-1) or its humanized form (hMN-14), as well as the anti-colon-specific antigen-p MAb, Mu-9. Imaging was performed from 4 to 240 h p.i. (planar and SPECT). The targeting kinetics and cumulated activity of tumors and organs were detd. from imaging data and blood clearance. Doses were calcd. according to the MIRD schema. An inverse logarithmic relationship between tumor size and MAb uptake was found for both anti-CEA Mabs (i.e., the smaller the lesion, the higher the uptake; uptakes ranging from 10-3 to 1% ID/g, doses from 0.3-59.5 mGy/MBq [1-220 rad/mCi]), whereas no such relationship was found for Mu-9. Tumor uptake was the most important factor detg. the dose (r=0.91), with the biol. half-time of the MAb in the tumor (range 21-398 h) being the next most important dose-detg. factor (r=0.51). The tenfold difference in affinity did not lead to significant differences in tumor uptake between both anti-CEA Mabs, but to longer biol. tumor

half-times of MN-14 as compared to NP-4. Colorectal and medullary thyroid cancers had higher tumor uptakes and tumor-to-red marrow dose ratios than other cancers ($p<0.01$). Maximal tumor uptake occurred between 4 and 48 h p.i., correlating to differences in the blood half-times. Biol. blood and tumor half-times of the anti-CEA Mabs were significantly shorter in colorectal than in other cancers. HAMA decreased the tumor uptake and tumor-to-non-tumor ratios by increasing MAb clearance. HAHA (anti-human=anti-idiotypic) antibodies had no effect on the biodistribution, but selectively decreased tumor uptake, and thus the dose. These data suggest that the tumor uptake is the most important dose-detg. factor. Differences in affinity are reflected by different half-times, not uptake values. In contrast to HAMA, HAHA seems to affect exclusively the tumor uptake without influencing the overall biodistribution. Esp. favorable conditions for anti-CEA antibodies seem to prevail in colorectal and medullary thyroid cancer, as well as patients with minimal disease, where cytotoxic tumor doses may be expected and therapeutic responses have been obtained.

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2010 ACS on STN
AN 1997:233151 CAPLUS
DN 126:290140
OREF 126:56105a,56108a
TI Variables influencing tumor dosimetry in radioimmunotherapy of CEA-expressing cancers with anti-CEA and antimucin monoclonal antibodies
AU Behr, Thomas M.; Sharkey, Robert M.; Juweid, Malik E.; Dunn, Robert M.; Ying, Zhiliang; Zhang, Cun-H.; Siegel, Jeffry A.; Goldenberg, David M.
CS Garden State Cancer Center at the Center for Molecular Medicine and Immunology, Newark, NJ, 07109, USA
SO Journal of Nuclear Medicine (1997), 38(3), 409-418
CODEN: JNMEAQ; ISSN: 0161-5505
PB Society of Nuclear Medicine
DT Journal
LA English

AB In this study, we examd. the factors that may influence tumor dosimetry in the radioimmunotherapy of solid, CEA-expressing cancers. Data from 119 tumors in 93 patients with CEA-expressing cancers were analyzed. The patients underwent radioimmunotherapy with the 131I-labeled IgG1 anti-CEA antibodies NP-4 (Ka = 108M-1) or MN-14 (Ka = 109 M-1), its humanized form hMN-14, as well as the anticolon-specific antigen-p (CSAp) antibody, Mu-9. For dosimetry, the biodistribution, targeting kinetics and cumulated activity of tumors and organs were detd. from planar and SPECT imaging. An inverse logarithmic relationship between tumor size and antibody uptake was found for both anti-CEA antibodies,

whereas no such relationship was found for Mu-9. The abs. tumor uptake
was identified as the most important factor detg. the radiation dose to
the tumor (r = 0.9), with the biol. half-life of the antibody in the tumor
being of secondary importance (r = 0.5). No significant difference in
tumor uptake was found between both anti-CEA antibodies, despite their
tenfold difference in affinity. At comparable masses, colorectal
and medullary thyroid cancers had significantly higher tumor
uptakes (p = 0.02), as well as tumor-to-red marrow dose ratios, than other
cancer types. The tumor half-lives of the anti-CEA antibodies were
significantly lower in colorectal than in all other tumor types
(p = 0.01). In radioimmunotherapy, tumor uptake appears to be the most
important dose-detg. factor. Differences in antibody affinity are
reflected by differences in the biol. half-life, not the abs. uptake.
Esp. favorable conditions for anti-CEA antibodies seem to prevail in
colorectal cancer patients having minimal disease, as well as in
medullary thyroid cancer, where cytotoxic tumor doses might be
expected. Antimucin antibodies may have a particular advantage in the
treatment of patients with larger colorectal tumors.

OSC.G 42 THERE ARE 42 CAPLUS RECORDS THAT CITE THIS RECORD (42 CITINGS)

L7 ANSWER 4 OF 4 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN

AN 1996:24190 BIOSIS

DN PREV199698596325

TI Evaluation of a complementarity-determining region-grafted (humanized)
anti-carcinoembryonic antigen monoclonal antibody in preclinical and
clinical studies.

AU Sharkey, Robert M.; Juweid, Malik; Shevitz, Jerry; Behr, Thomas; Dunn,
Robert; Swayne, Lawrence C.; Wong, George Y.; Blumenthal, Rosalyn D.;
Griffiths, Gary L.; Siegel, Jeffry A.; Leung, Shui-On; Hansen, Hans J.;
Goldenberg, David M. [Reprint author]

CS CMMI, 1 Bruce St., Newark, NJ 07103, USA

SO Cancer Research, (1995) Vol. 55, No. 23 SUPPL., pp. 5935S-5945S.
CODEN: CNREA8. ISSN: 0008-5472.

DT Article

LA English

ED Entered STN: 12 Jan 1996
Last Updated on STN: 12 Jan 1996

AB A complementarily-determining region-grafted (humanized) version of MN-14
(hMN-14), a high-affinity. anti-carcinoembryonic
antigen (CEA) murine monoclonal antibody (mMAb), was selected from several
clones that differed slightly in their framework composition. One clone
was selected based on its similar binding affinity to CEA as that observed
with mMN-14 MAb and its production yields. Targeting studies, using
131I-labeled humanized MN-14 (hMN-14)/125I-labeled

mMN-14 IgG in GW-39 tumor-bearing nude mice, showed excellent tumor uptake and tumor: nontumor ratios, similar to the mMN-14. A pilot clinical imaging trial was initiated to determine the targeting, pharmacokinetics, and dosimetry for 131I-labeled hMN-14 IgG. Nineteen patients with advanced CEA-producing tumors were given 8 to 30 mCi (0.5 to 20.0 mg). Eleven patients also received 131I-labeled mMN-14 IgG for comparison. The biodistribution, tumor targeting, and pharmacokinetic behavior of the hMN-14 was similar to that seen with the mMN-14. The average time required to clear 50% of the radiolabeled hMN-14 from the blood and total body was 32.9 25.6 h and 109 +- 73 h, respectively. Patients with elevated plasma CEA (i.e., gt 200 ng/ml) had more than 30% of the labeled antibody complexed within I h after injection. In some of these patients, increased complexation resulted in enhanced metabolism of the antibody with more rapid clearance from the blood than that seen in patients with lower plasma CEA. The average radiation absorbed dose measured in 20 tumors (average weight, 204 +- 205 g) in 14 patients was 7.6 +- 5.3 cGy/mCi. Tumor: nontumor dose ratios were 2.5 +- 1.6, 9.5 +- 5.8, and 2.6 +- 1.8 for the red marrow, total body, and liver, respectively. One patient, with a highly elevated human anti-mouse antibody response from a prior OncoScint study (murine B72.3 IgG), received 3 injections of the hMN-14 without an adverse experience, and showed no evidence of altered biodistribution characteristic of mMAb-human anti-mouse antibody interactions. An antibody response to hMN-14 (HAhMN14) was not detected in patients who received only the hMN-14 (as many as three injections), but in three patients who received two injections of the mMN-14, a HAhMN14 response was detected. With similar, excellent targeting properties as the mMN-14 and the potential for reduced immunogenicity, hMN-14 is an attractive candidate for further clinical imaging and therapy applications.